Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claims 1 and 2. (Canceled)

3. (Previously Presented) The method of claim 40, wherein the retention layer comprises a particulate material.

4. (Currently Amended) The method of claim 3, wherein the particulate material of the retention layer consists of glass beads.

5. (Previously Presented) The method of claim 40, wherein the retention layer comprises a rigid retention material.

6. (Previously Presented) The method of claim 5, wherein the rigid retention material comprises sinter plates.

7. (Previously Presented) The method of claim 40, wherein the clarification reactor has a top and a bottom, wherein the retention layer is disposed inside the clarification reactor between the top and the bottom of the clarification reactor,

wherein the mixture comprising the precipitate and the lysate enters the top of the clarification reactor, and the lysate exits the bottom of the clarification reactor, with the precipitate being retained within the clarification reactor by the retention layer,

wherein in step d), increasing pressure is applied at the top of the clarification reactor to the mixture comprising the precipitate and the lysate, thereby ensuring a constant outflow of the lysate from the bottom of the clarification reactor.

8. (Currently Amended) The method of claim [[7]] 48, wherein pressure is increased by applying pressurized air.

9. (Previously Presented) The method of claim 40, wherein one or more wash steps are inserted between steps d) and e).

10. (Canceled)

11. (Currently Amended) The method of claim 40, wherein the flow of the cell suspension and the flow of the lysis solution are combined, without further mixing, before entering the lysis reactor, thus forming a single flow within the lysis reactor that is ~~thoroughly~~ homogeneously mixed when flowing through the ~~particulate material~~ filling elements in the lysis reactor.

12. (Previously Presented) The method of claim 40, wherein the cell suspension and the lysis solution are introduced into the lysis reactor in the form of two independent flows.

13. (Currently Amended) The method of claim 12, wherein the two flows are introduced from independent sources connected through a T-type or Y-type connector[[s]], thus forming a single flow.

14. (Currently Amended) The method of claim 12 or 13, wherein the two flows are transported at a defined ratio of flow rates, the flow rates being regulated by pressure or pumps, thereby ensuring a constant ratio of cell suspension and lysis solution volumes.

15. (Previously Presented) The method of claim 40, wherein in step c), the lysed cell solution obtained in step b) is mixed with the neutralization solution in a continuous mode.

16. (Previously Presented) The method of claim 15, wherein the lysed cell solution and the neutralization solution are combined at a constant ratio of flow rates.

17. (Previously Presented) The method of claim 40, wherein a concentration and/or a conditioning step is inserted between step d) and step e).

18. (Previously Presented) The method of claim 17, wherein a concentration step and a condition step are inserted, and wherein said concentration step takes place before said conditioning step.

19. (Previously Presented) The method of claim 40, wherein said biomolecule of interest is a polynucleotide.

20. (Previously Presented) The method of claim 19, wherein the polynucleotide is plasmid DNA.

Claims 21 and 22. (Canceled)

23. (Previously Presented) The method of claim 40 wherein, in addition, step a) is operated in a continuous mode.

24. (Previously Presented) The method of claim 40, wherein the cell suspension obtained in step a) is cryo-pelleted.

Claims 25 – 39 (Canceled)

40. (Currently Amended) A method of purifying a biomolecule of interest from a host cell using an automated or semi-automated device, wherein the device comprises a lysis reactor, a neutralizing reactor and a clarification reactor fluidly connected to one another, the method comprising:

a) providing ~~cultivating host cells to produce the biomolecule of interest and forming~~ a cell suspension of ~~the cultivated~~ host cells that have been cultivated to produce the biomolecule of interest, wherein the cell suspension is a fermentation broth within which ~~containing~~ the ~~cultivated~~ host cells were cultivated or a re-suspension of the cultivated host cells that [[are]] were harvested from the fermentation broth;

b) introducing a flow of the cell suspension and a flow of a lysis solution into [[a]] the lysis reactor, wherein the lysis reactor contains filling elements made of glass, plastic, stainless steel or fibrous material, wherein the flow of the cell suspension and the flow of the lysis solution are homogenously mixed as a result of flowing through the filling elements in the lysis reactor so that irreversible denaturation of the biomolecule of interest is avoided and ~~at a defined ratio of flow rates and disintegrating~~ the cultivated host cells are disintegrated by alkaline lysis in the absence of shear forces in the lysis reactor to produce a lysed cell solution~~, wherein the lysis reactor contains a particulate material~~;

c) ~~neutralizing, in a neutralization reactor,~~ transporting the lysed cell solution via the neutralization reactor wherein the lysed cell solution is mixed with a neutralization solution to produce a mixture comprising a lysate and a precipitate comprising cellular debris and impurities, and wherein the lysate contains the biomolecule of interest~~, and wherein the neutralization reactor is fluidly connected to the lysis reactor and the lysed cell solution is mixed with a neutralization solution in the neutralization reactor~~;

d) ~~separating, in a clarification reactor,~~ introducing the mixture comprising the precipitate and the lysate into the clarification reactor wherein the lysate containing the biomolecule of interest is separated from the precipitate, wherein ~~the neutralization reactor is fluidly connected to the clarification reactor so that~~ the mixture comprising the precipitate and the lysate is allowed to flow through the clarification reactor, and wherein the clarification reactor contains a retention layer that functions to ~~separate~~ retain the precipitate [[from]] but allow the lysate ~~so that the precipitate is retained by the retention layer and the lysate is allowed~~ to [[to]] flow from the clarification reactor; and

e) purifying the biomolecule of interest, where the biomolecule of interest is purified from the lysate that flows from the clarification reactor,

wherein said method is operated on a manufacturing scale.

41. (Previously Presented) The method of claim 40, wherein one or more distribution means are disposed inside the clarification reactor and extend to a surface of the retention layer, wherein the one or more distribution means evenly distribute the mixture comprising the precipitate and the lysate as obtained in step c) into the clarification reactor of step d).

42. (Currently Amended) The method of claim 40, wherein the filling elements are a particulate material ~~consists of glass beads~~.

43. (Previously Presented) The method of claim 7, wherein the retention layer has a top facing the top of the clarification reactor and a bottom facing the bottom of the clarification reactor, wherein the retention layer functions to retain the precipitate on the top of and within the retention material while allowing the purified lysate to flow from the clarification reactor.

44. (Currently Amended) The method of claim [[40]] 42, wherein ~~the lysis reactor is essentially completely filled with~~ the particulate material consists of beads, each bead having a diameter in the range of about 1 to about 100 mm.

45. (New) The method of claim 44, wherein each bead has the same diameter.

46. (New) The method of claim [[40]] 42, wherein the lysis reactor is essentially completely filled with the particulate material.

47. (New) The method of claim 42, wherein in the particulate material consists of glass beads.

48. (New) The method of claim 7, wherein pressure is increased by applying pressurized gas.